CASE 4-33179

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE: US Patent Number 5,096,890
ISSUED: March 17, 1992
TO: Peter E. Cross and Alexander R. MacKenzie
FOR: PYRROLIDINE DERIVATIVES

Box Patent Extension
Assistant Commissioner for Patents
Washington, D.C. 20231

PATENT TERM EXTENSION APPLICATION UNDER 35 USC § 156

Sir:

Pursuant to 35 U.S.C. §156 and 37 C.F.R. §1.710 *et seq.*, Novartis International Pharmaceutical Ltd., a company organized and existing under the laws of the Island of Bermuda, hereby requests an extension of the patent term due to regulatory review of U.S. Patent No. 5,096,890, which was granted on March 17, 1992.

Applicant, Novartis International Pharmaceutical Ltd., a company organized and existing under the laws of the Island of Bermuda, and having a place of business at 48 Church Street, Sofia House, Hamilton HM 12, Bermuda, represents that it is the owner of the entire title and interest in and to U.S. Patent No. 5,096,890 which was granted on March 17, 1992 to Peter E. Cross and Alexander R. MacKenzie for "PYRROLIDINE DERIVATIVES" by virtue of assignments in favor of:

1. Pfizer, Inc from and by Peter E. Cross and Alexander R. MacKenzie on April 24, 1990, which assignment is recorded in the United States Patent and Trademark Office at Reel 5289, Frame 0385;

and a subsequent assignment to

2. Novartis International Pharmaceutical, Ltd. from and by Pfizer, Inc. on November 5, 2003, which assignment is recorded in the United States Patent and Trademark Office at Reel 014709, Frame 0987.

Applicant appoints, by Power of Attorney, attached hereto as "Appendix A" the undersigned counsel, Edward J. Wilusz, Jr. and Susan Hess to act as its attorneys in this matter and also appoints the attorneys and agents associated with Customer No. 001095, respectively and individually, with regard to this application for extension of the term of U.S. Patent No. 5,096,890 and to transact all business in the U.S. Patent and Trademark Office in connection therewith.

1. Identification of the Approved Product under 37 CFR §1.740(a)(1)

The complete identification of the approved product is:

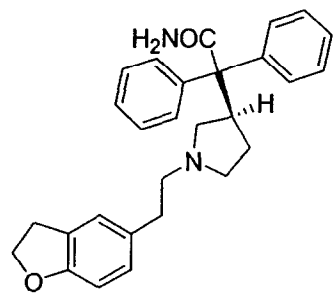
chemical name: (S)-2-{1-[2-(2,3-dihydrobenzofuran-5-yl)ethyl]-3-pyrrolidinyl}-2,2-diphenylacetamide hydrobromide

also known as: DAR 328A or EMSELEX (European Union)

Tradename: ENABLEX ®

generic name: darifenacin hydrobromide

chemical structure:



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2. Identification of the Federal Statute under which Regulatory Review Occurred under 37 CFR §1.740(a)(2)

The approved product was subject to regulatory review under the Federal Food, Drug and Cosmetic Act Section 505 (21 USC §355).

3. The Date of Permission for Commercial Marketing under 37 CFR §1.740(a)(3)

The approved product received permission for commercial marketing or use under Section 505 of the Federal Food, Drug and Cosmetic Act (21 USC §355) on December 22, 2004.

4. Active Ingredient Statement under 37 CFR §1.740(a)(4)

The sole active ingredient in ENABLEX® is darifenacin hydrobromide; and darifenacin, or any other pharmacologically acceptable salt thereof, has not been previously approved for commercial marketing or use under the Federal Food, Drug and Cosmetic Act section 505 (21 USC § 355) prior to the approval of NDA 21-513 by the United States Food and Drug Administration on December 22, 2004.

5. Statement of Timely Filing under 37 CFR §1.740(a)(5)

This Application for Extension of the term of U.S. Patent No. 5,096,890 under 35 USC §156 is being submitted within the permitted 60 day period set forth in 37 CFR §1.720(f), which period will expire on February 20, 2005.

6. Identification of Patent for which Extension is Sought under 37 CFR §1.740(a)(6)

The patent, the term of which this Application seeks to extend, is: U.S. Patent No. 5,096,890 which issued on March 17, 1992 to Peter E. Cross and Alexander R. MacKenzie, the term of which would otherwise expire on March 13, 2010. Claims 1 through 9 of U.S. Patent No. 5,096,890 apply to the approved product, ENABLEX®, as approved for marketing in the United States by the U.S. Food and Drug Administration.

7. Patent Copies under 37 CFR §1.740(a)(7)

A complete copy of U.S. Patent No. 5,096,890, identified in paragraph 6 above, is attached as "Appendix B".

8. Post Issuance Activity Statement under 37 CFR §1.740(a)(8)

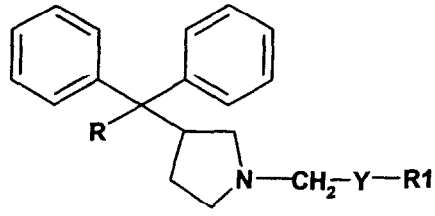
A Re-examination Certificate B1 5,096,890 (Number 2512th), issued on March 28, 1995, is included as "Appendix C". The result of the Re-examination is that no amendments were made to U.S. Patent No. 5,096,890 and the patentability of claims 1 through 10 (all claims) is confirmed. No Certificate of Correction, Terminal Disclaimer, or Re-Issue has been issued or requested with respect to U.S. Patent No. 5,096,890. The First Maintenance Fee for U.S. Patent No. 5,096,890, in the amount of $960.00, has been paid, the Second Maintenance Fee in the amount of $1,900.00 has been paid, and the Third Maintenance Fee, in the amount of $3,150.00 has been paid. Copies of the Maintenance Fee Statements for the First, Second, and Third Maintenance Fees are attached hereto as "Appendix D".

9. Statement Showing How the Claims of the Patent for which Extension is Sought Cover the Approved Product under 37 CFR §1.740(a)(9)

The claims 1 through 9 of U.S. Patent No. 5,096,890 cover certain specific pyrrolidine derivatives, per se, their pharmacologically acceptable salts, which include the active ingredient of ENABLEX®, (S)-2-{1-[2-(2,3-dihydrobenzofuran-5-yl)ethyl]-3-pyrrolidinyl}-2,2-diphenylacetamide hydrobromide, pharmaceutical compositions comprising said compounds, which include the marketed composition of ENABLEX®, and the use of said compounds for treating various diseases, which include the approved indication for ENABLEX®. An example of how ENABLEX® is included in the scope of claims 1-9 of U.S. Patent No. 5,096,890, as required under 37 CFR §1.740(a)(9)(i) et seq. follows:

Claim 1 of U.S. Patent No. 5,096,890 reads as follows:

1. A compound of the formula:

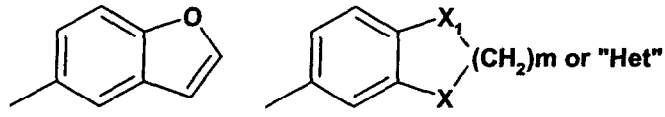


or a pharmaceutically acceptable salt thereof, wherein

Y is a direct link, $-CH_2-$, $-(CH_2)_2-$, $-CH_2O-$ or $-CH_2S-$;

R is $-CONH_2$; and

R1 is a group of the formula:

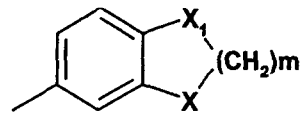


where X and X_1 are each independently O or CH_2;

m is 1, 2 or 3; and

"Het" is pyridyl, pyrazinyl or thienyl.

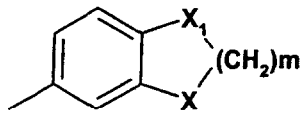
Since this claim covers the compound 2-{1-[2-(2,3-dihydrobenzofuran-5-yl)ethyl]-3-pyrrolidinyl}-2,2-diphenylacetamide, the optical isomers of said compound, i.e., the (S) and (R) isomers, and the pharmacologically acceptable salts of the compound and the individual isomers, the claim covers the

approved product ENABLEX ®. For example, when Y is -CH_2-, R1 is a group of the formula 

, where X is O, X_1 is CH_2, m is 1, and the compound is the (S) enantiomer in hydrobromide salt form, as allowed by the stated elements of claim 1, then the compound is (S)-2-{1-[2-(2,3-dihydrobenzofuran-5-yl)ethyl]-3-pyrrolidinyl}-2,2-diphenylacetamide hydrobromide. Thus, since the sole active ingredient in ENABLEX®, which is darifenacin hydrobromide, is the hydrogen bromide salt of the (S) isomer of 2-{1-[2-(2,3-dihydrobenzofuran-5-yl)ethyl]-3-pyrrolidinyl}-2,2-diphenylacetamide, the scope of Claim 1 of U.S. Patent No. 5,096,890 encompasses ENABLEX® is included within.

Claim 8 of U.S. Patent No. 5.096,890 is a composition claim and reads as follows:

8. A pharmaceutical composition comprising muscarinic receptor antagonizing effective amount of a compound according to claim 1 and a pharmaceutically acceptable diluent or carrier.

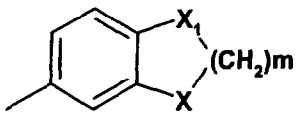
This claim covers a pharmaceutical composition of a muscarinic receptor antagonizing effective amount of a compound, which, as allowed by claim 1, includes (S)-2-{1-[2-(2,3-dihydrobenzofuran-5-yl)ethyl]-3-pyrrolidinyl}-2,2-diphenylacetamide hydrobromide when Y is -CH_2-, R1 is a group of the formula 

, where X is O, X_1 is CH_2, m is 1, and the compound is the (S) enantiomer in hydrobromide salt form, which compound is also darifenacin hydrobromide, which as, stated in the ENABLEX® product labelling, is a muscarinic receptor antagonist, and which composition also contains a pharmaceutically acceptable diluent or carrier such as, for example, hydroxypropylmethylcellulose and lactose monohydrate, which are examples of carriers or diluents that are included in the marketed formulation of ENABLEX® as stated in the ENABLEX® product labelling. Therefore, the approved pharmaceutical composition of ENABLEX® is included within the scope of claim 8 of U.S. Patent No. 5,096,890.

Claim 9 of U.S. Patent No. 5.096,890 reads as follows:

9. A method of treating a disease associated with altered motility or tone of smooth muscle in a mammal comprising administering to said mammal a muscarinic receptor antagonizing amount of a compound according to claim 1.

Claim 9 covers a method of treating a disease associated with altered motility or tone of smooth muscle in a mammal comprising administering to said mammal a muscarinic amount of a compound, which, as allowed by claim 1, includes (S)-2-{1-[2-(2,3-dihydrobenzofuran-5-yl)ethyl]-3-pyrrolidinyl}-2,2-diphenylacetamide hydrobromide when Y is $-CH_2-$, R1 is a group of the formula



, where X is O, X_1 is CH_2, m is 1, and the compound is the (S) enantiomer in hydrobromide salt form, which compound is also darifenacin hydrobromide, and which, as stated in the ENABLEX product labelling, is a muscarinic receptor antagonist. Further, the product labelling for ENABLEX® states that ENABLEX® (darifenacin) may be used or indicated to be administered to treat overactive bladder, which disease is known to be associated with altered motility or tone of smooth muscle in a mammal. Therefore, Claim 9 of U.S. Patent No. 5,096,890, encompasses the approved use or indication for ENABLEX®.

10. Statement of Relevant Dates to Determine the Regulatory Review Period under 37 CFR §1.740(a)(10)

The relevant dates and information pursuant to 35 USC §156(g) to enable the Secretary of Health and Human Services to determine the applicable regulatory review period are as follows:

a) An Investigational New Drug Application for darifenacin hydrobromide was received by the Department of Health and Human Services on June 13, 1994 and the IND number assigned was 45,457.

b) A New Drug Application was received by the Department of Health and Human Services on December 30, 2002 and the NDA number assigned was 21-513.

c) The date on which NDA 21-513 was approved was December 22, 2004. The unconditional NDA approval letter and approved labelling for ENABLEX® are attached as "Appendix E".

11. Brief Description of Significant Activities Undertaken During the Regulatory Review Period under 37 CFR §1.740(a)(11)

As a brief description of the activities undertaken during the applicable regulatory review period, attached hereto as "Appendix F" is a chronology of the major communications between the US Food and Drug Administration and the Applicant in the IND and NDA mentioned in paragraph 10 above.

12. Opinion of Eligibility for Extension under 37 CFR §1.740(a)(12)

Applicant is of the opinion that U.S. Patent No. 5,096,890 is eligible for extension under 35 USC §156 and 37 CFR §1.720 because it satisfies all of the requirements for such extension as follows:

(a) 35 USC §156(a) and 37 CFR §1.720(a)

U.S. Patent No. 5,096,890 claims a human drug product, darifenacin hydrobromide, and various compositions and methods of using the human drug product as defined in 37 CFR §1.710.

(b) 35 USC §156(a)(2) and 37 CFR §1.720(b)

The term of U.S. Patent No. 5,096,890 has never been extended.

(c) 35 USC §156(a)(3) and 37 CFR §1.720(c)

The Application for extension of the term of U.S. Patent No. 5,096,890 is submitted by the authorized agent of the owner of record thereof in accordance with the requirements of 35 USC §156(d) and 37 CFR §1.740.

(d) 35 USC §156(a)(4) and 37 CFR §1.720(d)

The approved product, ENABLEX ®, has been subjected to a regulatory review period, as defined in 35 U.S.C. §156(g), before its commercial marketing or use.

(e) 35 USC §156(a)(5) and 37 CFR §1.720(e)(i)

The product has received permission for commercial marketing and the permission for the commercial marketing is the first received permission for commercial marketing or use under the provision of law under which the applicable regulatory review occurred.

(f) 35 USC §156(d)(1) and 37 CFR §1.720(f)

The application for patent term extension is being submitted within the sixty-day period beginning on the date the product first received permission for commercial marketing (date of the unconditional NDA approval letter) under the provisions of law under which the applicable regulatory review period occurred.

(g) 35 USC §156(a)(1) and 37 CFR §1.720(g)

The term of U.S. Patent No. 5,096,890 (expiring March 13, 2010) has not expired before the submission of this application.

(f) 35 USC §156(a) and 37 CFR §1.720(h)

No other patent term has been extended for the same regulatory review period for the approved product, ENABLEX ®.

13. Length of Extension Claimed Under 37 CFR §1.740(a)(12)

The length of extension of the patent term of U.S. Patent No. 5,096,890 requested by Applicant is 2298 days, which length was calculated in accordance with 37 CFR §1.775 as follows:

(a) The regulatory review period under 35 USC §156(g)(1)(B) began on June 13, 1994 (the confirmation date of receipt and the IND by the FDA) and ended on December 22, 2004, amounting to a total of 3,845 days or 10.56 years, which is the sum of (i) and (ii) below:

(i) The period of review under 35 USC §156(g)(1)(B)(i), the "Testing Period", began on June 13, 1994 and ended on December 2, 2002, which is 3,094 days or 8.48 years;

(ii) The period for review under 35 USC §156(g)(1)(B)(ii) the "Application Period", began on December 2, 2002 and ended on December 22, 2004, which is 751 days or 2.06 years;

(b) The regulatory review period upon which the period for extension is calculated is the entire regulatory review period as determined in sub-paragraph (13)(a) above (3845 days) less:

(i) The number of days in the regulatory review period which were on or before the date on which the patent issued (March 17, 1992), i.e. zero days, and

(ii) The number of days during which the Applicant did not act with due diligence, i.e., zero days, and

(iii) One half of the number of days remaining in the period in subparagraph (13)(a)(i) after subtracting the number of days in subparagraphs (13)(b)(i) and (13)(b)(ii), which is one half of (3094 - [0+0]) or 1547 days;

which results in a period of 3845 - [0+0+1547] = 2298 days or 6.30 years.

(c) The number of days as determined in sub-paragraph (13)(b), when added to the original term, would result in the date of June 27, 2016.

(d) Fourteen (14) years when added to the date of the unconditional NDA Approval Letter (December 22, 2004) would result in the date of December 22, 2018.

(e) The earlier date as determined by sub-paragraphs (13)(c) and (13)(d) is June 27, 2016.

(f) Since the original patent was issued after September 24, 1984, the extension otherwise obtainable is limited to not more than five years. Five years, when added to the original expiration of U.S. Patent No. 5,096,890 (March 13, 2010) results in the date of March 13, 2015.

(g) The earlier date as determined in sub-paragraphs (13)(e) and (13)(f) is March 13, 2015.

14. Duty of Disclosure Acknowledgment under 37 CFR §1.740(a)(13)

Applicant acknowledges a duty to disclose to the Commissioner of Patents and Trademarks and the Secretary of Health and Human Services any information which is material to the determination of entitlement to the extension sought.

15. Prescribed Fee Charge

The prescribed fee for receiving and acting upon this application is to be charged to Applicant's Deposit Account 19-0134 as authorized in the attached transmittal letter, submitted in triplicate.

16. Correspondence Address Required by 37 CFR §1.740(a)(15)

All correspondence relating to this application for patent term extension should be addressed to:

Novartis
Corporate Intellectual Property
One Health Plaza, Building 104
East Hanover, NJ 07936-1080

Additional Inquiries may be made by telephone to the undersigned counsel at the telephone number listed below.

Respectfully submitted,

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Reg. No. 52,370

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Date: February 18, 2005

Susan Hess
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Date: February 18, 2005